REMARKS

The Amendment, filed in response to the Office Action mailed October 27, 2010, address all and every issue raised in the Office Action. Favorable reconsideration on the merits and allowance of the application are respectfully requested.

Disposition of Claims

In the Office Action, claims 1-7, 13 and 15 were considered and rejected.

In the instant Amendment, claims 1, 6, and 13 are amended to more clearly set forth the claimed subject matter. No claims are canceled.

Therefore, upon entry of the amendment, which is respectfully requested, claims 1-13 and 15 will be all claims pending in the application. Claims 8-12 have been withdrawn from consideration as being directed to non-elected subject matter.

Withdrawn Rejections

Applicants thank the Examiner for withdrawing the rejection under 35 U.S.C. 102(b) over Maddon, and the rejection under 35 U.S.C. 103(a) based on Maddon and Presta.

Response to Rejection Under 35 U.S.C. 112, second paragraph

In the Office Action, claims 1-7, 13, and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite, because the metes and bounds of the "combination thereof or a hybrid thereof' is allegedly ambiguous.

In the Office Action, claim 6 is rejected as being indefinite assertedly because, in the recitation of "IgG4 Fc fragment is human-derived," it is not clear how an Fc fragment can be derived from human.

In response, without conceding the rejections, solely for the Applicants' interest of compact prosecution, claims 1 and 6 are amended, rendering the rejection moot. Withdrawal of the rejections is respectfully requested.

Response to Rejections Under 35 U.S.C. 112, First Paragraph

1. Claim 13

In the Office Action, claim 13 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. In particular, the term "pharmaceutical" of the recitation "pharmaceutical composition" was pointed out by the Examiner as raising an enablement issue. The Examiner kindly suggests amending the term to remove the word "pharmaceutical."

In response, without conceding the rejection, solely in order to advance the prosecution, claim 13 is amended as suggested by the Examiner, rendering the rejection moot. Withdrawal of the rejection is respectfully requested.

2. Claims 1-7, 13 and 15

In the Office Action, claims 1-7, 13, and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. In particular, the recitation "wherein the non-peptide linker comprises polyethylene glycol … or combination thereof' is pointed out by the Examiner as raising a new matter issue.

Without acquiescing the rejection, solely for the interests of Applicants to advance the prosecution, Applicants amend claim 1 as shown above, rendering the rejection moot. Withdrawal of the rejection is respectfully requested.

Response to Rejection under 35 U.S.C. 102(e)

1. Rejection Summary

In the Office Action, claims 1-7, 13, and 15 are rejected under 35 U.S.C. 102(e) as assertedly being anticipated by Kostenuik et al. (US Patent 6,756,480).

The Examiner asserts that Kostenuik et al. teach parathyroid hormone peptide (PHP) covalently linked to an Fc domain via a linker (e.g. see claims 1-3). The Examiner further relies on the definitions of Linkers provided on columns 33-34 of Kostenuik et al to assert that the linker of Kostenuik can be non-peptide linker such as PEG linker.

2. Applicants' Arguments

Applicants respectfully traverse.

It is noted that Kostenuik et al disclose that a. linker can be non-peptide linker such as a PEG linker (column 34). The relevant portion of Kostenuik provides a long list of linkers which can be used and the linker may be a peptide or non-peptide.

Kostenuik does not disclose a working example of a protein conjugate in which an Fc fragment is covalently linked to a drug through a non-peptide linker, or discloses any embodiment of the drug-non-peptide linker. The mere fact that a single reference teaches all elements is not sufficient to anticipate a claimed subject matter, when the teachings of each element is scattered and the single reference fails to teach the elements arranged in the same

matter as defined in claim. Therefore, Applicants respectfully submit that Kostenuik fails to anticipate the subject matter recited in claim 1.

In addition, Applicants respectfully submit that Kostenuik fails to provide guidance or motivation to combine the elements taught therein in a manner to reach the claimed subject matter. Kostenuik fails to recognize any advantage of using a non-peptide linker in a conjugate of a Fc fragment, a non-peptide linker, and a physiologically active polypeptide. Rather, *Kostenuik* states that the *linker is preferably made up of amino acids linked together by peptide bonds* (columns 33 lines 50-53). Furthermore, Kostenuik et al states that "An Fc domain is the preferred vehicle, the Fe domain may be fused to the C terminus of the peptide.... In such Fc variants, one may remove these sites of a native Fc that provide structural features or functional activity not required by the fusion molecules of this invention. " (columns 31. lines 33-42), and "The compounds of this invention largely may be made in transformed host cells using recombinant DNA techniques" (column 36 lines 58-59). Kostenuik et al also states that all of the compounds of their invention can be prepared by the methods described in PCT Appl. No. W099/25044 (column 45 lines 36-37), which discloses details of an Fc fusion technique and fusion protein prepared by expressing a physiologically active polypeptide and Fc fragment coincidentally using one expression vector in one expression cell.

One skilled in the art would understand from reading the above-discussed disclosures of Kostenuik, Kostenuik teaches that a non-peptide linker should be used together with an additional vehicle such as a polymer (e.g. PEG or dextran), while a peptide linker would be used together with a peptide vehicle which is in the Fc domain (column 8 lines 42-57).

In contrast, the currently presented claim 1 clearly excludes a peptide linker. Currently presented claim 1 requires that the Fc region is covalently linked to a drug through a non-peptide linker, and the linker is the non-peptide linker is polyethylene glycol, polypropylene glycol, copolymers of ethylene glycol and propylene glycol, polyoxyethylated polyols, polyvinyl alcohol, dextran, polyvinyl ether, polylactic acid (PLA), polylactic- glycolic acid (PLGA), a lipid polymer, a chitin, or hyaluronic acid.

According to the present application, the Fc fragment and the physiologically active polypeptide can be prepared separately, and then the separately prepared Fc fragment and physiologically active polypeptide are covalently linked through a non-peptide polymer. Only the present invention makes it possible to produce a conjugate of a glycosylated active polypeptide and an aglycosylated imunoglobulin Fc fragment, and overcomes the problems associated with known Fc fusion proteins, including improving protein production yield.

Accordingly, the rejection is not sustainable and its withdrawal is respectfully requested.

Response to Provisional ODP Rejections

In the Office Action, claims 1-7, 13, and newly added 15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of copending USSN 10/535,231 and claims 1-19 and 27-45 of copending USSN 10/535,232 for reasons of record.

In the Office Action, claims 1-7, 13, and newly added 15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-

19 and 24 of copending USSN 11/747,153 and claims 1-25 of copending USSN 11/910,962 and claims 1- 26 and 33 of copending USSN 11/947,697.

Claims 1-7, 13 and 15 are directed to an invention not patentably distinct from claims 1-19 and 24 of commonly assigned copending USSN 11/747,153 and claims 1-25 of commonly assigned copending USSN 11/910,962 and claims 1-26 and 33 of commonly assigned copending USSN 11/947,697 for reasons stated above.

Applicants hereby respectfully request the Examiner to hold the rejection abeyance until any patentable subject matter is identified.

Statement of Common Ownership

The Examiner states that commonly assigned USSN 11/747,153, 11/910,962, and 11/947,697 would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. The Examiner also advises that the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

In response, Applicant hereby states that the inventions of US Serial Numbers 11/747,153, 11/910,962, and 11/947,697 and the invention of the instant application were commonly owned at the time the invention in the instant application.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number **202-775-7588**.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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